ACTG2 gene

actin, gamma 2, smooth muscle, enteric

Normal Function

The *ACTG2* gene provides instructions for making a protein called gamma (γ)-2 actin, which is part of the actin protein family. Actin proteins are organized into filaments, which are important for the tensing of muscle fibers (muscle contraction) and cell movement. These filaments also help maintain the cytoskeleton, which is the structural framework that determines cell shape and organizes cell contents.

The γ-2 actin protein is found in smooth muscle cells of the urinary and intestinal tracts. Smooth muscles line the internal organs; they contract and relax without being consciously controlled. The γ-2 actin protein is necessary for contraction of the smooth muscles in the bladder and intestines. These contractions empty urine from the bladder and move food through the intestines as part of the digestive process.

Health Conditions Related to Genetic Changes

Intestinal pseudo-obstruction

Several inherited mutations in the *ACTG2* gene have been identified in people with intestinal pseudo-obstruction, a condition that impairs the smooth muscle contractions that move food through the digestive tract (peristalsis). This condition mimics a physical blockage of the intestines without an actual obstruction. Problems with emptying the bladder can also occur in people with this disorder.

The *ACTG2* gene mutations that cause intestinal pseudo-obstruction are thought to hinder the formation of actin filaments in the cytoskeleton and reduce the ability of smooth muscles in the intestines and bladder to contract. As a result, peristalsis in the intestines is impaired and the bladder is less able to contract and expel urine, leading to the signs and symptoms of this condition.

Megacystis-microcolon-intestinal hypoperistalsis syndrome

At least 22 *ACTG2* gene mutations have been found to cause megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS), which is characterized by impairment of peristalsis and emptying the bladder.

The *ACTG2* gene mutations that cause MMIHS are not inherited; rather they occur as a random (de novo) event during the formation of reproductive cells (eggs or sperm) or in early embryonic development. The alterations change single protein building blocks (amino acids) in the γ-2 actin protein. These changes hinder the formation of

actin filaments and reduce the ability of smooth muscles in the bladder and intestines to contract. As a result, the bladder cannot empty normally, leading to an enlarged bladder (megacystis) and painful abdominal swelling (distention). In addition, partially digested food can build up in the intestines, which also contributes to distention. Poor digestion may lead to malnutrition in people with MMIHS.

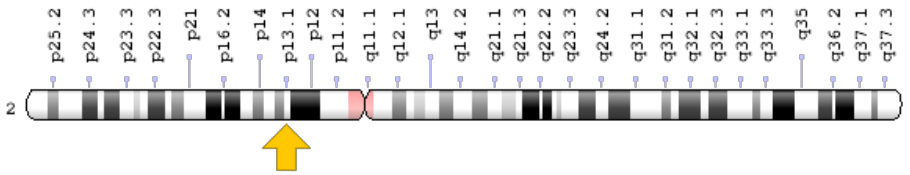
Other disorders

ACTG2 gene mutations cause a spectrum of disorders (sometimes referred to as *ACTG2*-related disorders), with MMIHS (described above) at the severe end. As in MMIHS, most of these mutations change single amino acids in the γ-2 actin protein. However, in less severely affected individuals, the mutations are usually inherited. These mutations often cause intestinal pseudo-obstruction (described above). In some affected individuals, the smooth muscle problems are episodic and come and go throughout life. Intestinal malrotation can also occur in people with *ACTG2* gene mutations. This condition occurs when the intestines do not fold properly; instead, they twist abnormally, which can impede the movement of food. Effects on the urinary tract include recurrent urinary tract infections and impaired bladder function. Individuals with inherited *ACTG2* gene mutations can have one or more of these intestinal or urinary tract abnormalities; they are usually milder than MMIHS, or they begin later in life. It is unclear why inherited and de novo mutations result in conditions with different severities.

Chromosomal Location

Cytogenetic Location: 2p13.1, which is the short (p) arm of chromosome 2 at position 13.1

Molecular Location: base pairs 73,893,008 to 73,919,865 on chromosome 2 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ACT
- ACTA3
- ACTE

- actin-like protein
- actin, gamma-enteric smooth muscle isoform 1 precursor
- actin, gamma-enteric smooth muscle isoform 2 precursor
- ACTL3
- ACTSG
- alpha-actin-3
- VSCM

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Smooth Muscles Contain Loosely Organized Thick and Thin Filaments
  https://www.ncbi.nlm.nih.gov/books/NBK21670/#_A5206_

Clinical Information from GeneReviews

- ACTG2-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK299311
- Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome Overview
  https://www.ncbi.nlm.nih.gov/books/NBK540960

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ACTG2%5BTIAB%5D%29+OR+%28%28actin,+gamma-enteric+smooth+muscle+isoform+1+precursor%5BTIAB%5D%29+OR+%28actin,+gamma-enteric+smooth+muscle+isoform+2+precursor%5BTIAB%5D%29+OR+%28actin-like+protein%5BTIAB%5D%29+OR+%28alpha-actin-3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ACTIN, GAMMA-2, SMOOTH MUSCLE, ENTERIC
  http://omim.org/entry/102545

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ACTG2.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ACTG2%5Bgene%5D

- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:145
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:72
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/72
- UniProt
  https://www.uniprot.org/uniprot/P63267

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